**Indo Global Journal of Pharmaceutical Sciences, 2012; 2(4): 351-367**

INDO GLOBAL JOURNAL OF PHARMACEUTICAL SCIENCES
**ISSN 2249- 1023**

# Suzuki Cross Coupling Reaction- A Review

Sarbjeet Singh Gujral, Smriti Khatri*, Poornima Riyal, Vinod Gahlot

*Maharaja Surajmal Institute of Pharmacy, Janakpuri, New Delhi, India*

**Address for Correspondance**: smriti_dua@yahoo.com

**ABSTRACT:** Suzuki cross coupling reaction is one of the most famous reaction in the field of chemistry. It is a very effective method for making carbon – carbon bonds. It has been extensively utilized in the synthesis of many carbon molecules including the most complex ones. It also find application in the synthesis of compounds of biological sources like (+)-dynemicin, Adragmacidin F, Flurbiprofen, Felbinac, Fenbufen, Difunisal, Aporphinoids, Oximidine II, Nemertelline, Gymnocin A, Palytoxin, Michellamine, CP-263,114, Halenaquinone, Brevetoxin, Yuehchukene, caparratriene etc which have been synthesized using the same reaction along with some other organic compounds. The present review article emphasis on carbon-carbon bond formation via cross coupling reaction, mechanism and applications in a natural product synthesis. 

**KEYWORDS:** Suzuki Cross Coupling Reaction; Medicinal Chemistry; Bioactive Compounds.

## *INTRODUCTION*

In recent times Suzuki- miyaura reaction which is more commonly known as “Suzuki coupling reaction” is one of the most useful cross-coupling reactions between aryl or vinyl boronic acid with aryl or vinyl halides and and also with different reagents like alkenes, alkynes, amines, pseudohalides, metallorganic compounds etc. catalyzed by palladium (0) complexes.[1][2][3][4]. It is widely used in the production of olefins (including poly olefins also), styrenes and substituted biphenyls are among some common examples. Generally an alternative of boronic acid which is organotrifloroborate salts are in common use.

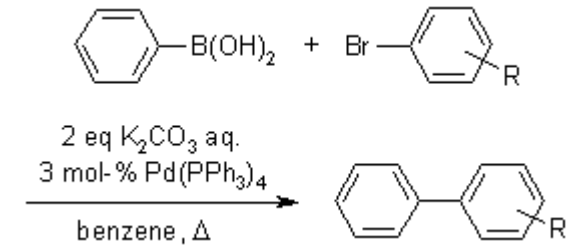
Palladium-catalyzed Suzuki cross coupling reactions are amongst the most powerful and most applicable method for C—C bond formation [5][6][7] . The reaction is generally carried out at temperatures range of 60–80°C with generally excellent yield results. Despite the availability of other cross coupling reaction like heck reaction, stille reaction to name a few, but due to various conditions like:

1) Milder reaction conditions.

2) Commercial availability of the diverse boronic acids derivatives that are environmentally safer than the other organometallic reagents.

3) The handling and removal of boron-containing byproducts is easy as compared to other organometallic reagents, especially in case of large-scale synthesis of a product.

So we can say that Suzuki cross coupling reaction has an edge over the other cross coupling reactions as this reaction is not only restricted to simple compounds but is frequently used in the production of complex compounds also. [8]



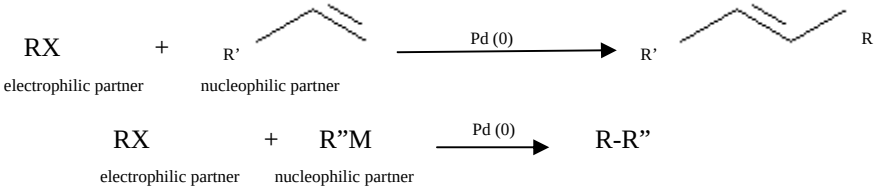

**An example of suzuki reaction**

***Role of Transition metals in organic chemistry***

In the late 20th century when extensive work on development of newer way of producing organic compounds was gaining interest among chemists, transition metals became the first choice of the chemists in organic chemistry synthesis which led to the development of a large number of transition metal-catalyzed reactions for the same. Transition metals can activate various organic compounds and through this activation they can catalyze the formation of new bonds. Palladium was the first known transition metal which was used in organic synthesis which can induce the formation of carbon- carbon bond on the account that ethylene was oxidized to acetaldehyde by air in a palladium-catalyzed reaction and this became the industrially important Wacker process[9]. Subsequent research on palladium-catalyzed carbonylation led to newer reactions for the formation of carbon-carbon bonds.

***Palladium-catalyzed carbon-carbon bond formation via cross coupling***

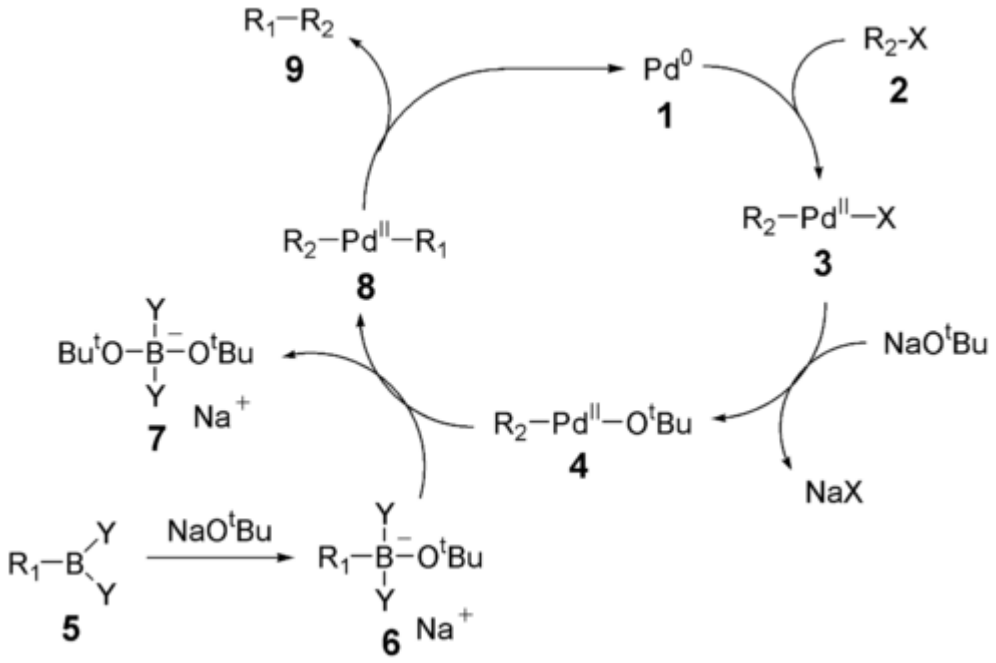
The principle mechanism of palladium-catalyzed cross couplings is that two molecules are adsorbed on the metal via the formation of metal-carbon bonds( an example of Heterogenous catalysis) . In this way the carbon atoms bound to palladium are brought very close to one another. In the next step they couple to one another and this leads to the formation of a new carbon-carbon single bond. There are two types of cross-coupling reactions according to this principle that have become important in organic synthesis. These two types of reactions are as follows:




Both reactions are catalyzed by zerovalent palladium and both reactions employ an organohalide RX (or analogous compound) as the electrophilic coupling partner. However, the nucleophilic coupling partner differs in the two reactions. In the first type of reaction it is an olefin whereas in the second type of reaction it is an organometallic compound R''M. A common feature of the two types of cross couplings is that the organic groups from the reagents are assembled on palladium. Furthermore, both reactions begin by generating an organopalladium complex RPdX from the reaction of the organic halide with Pd(0). The organopalladium species RPdX will subsequently react with the nucleophilic coupling partner (see detailed mechanisms below). The reactions are very mild since they utilize organic halides (or analogous compounds) and olefins or organometallic compounds R''M of low reactivity, where M is typically zinc, boron, or tin.

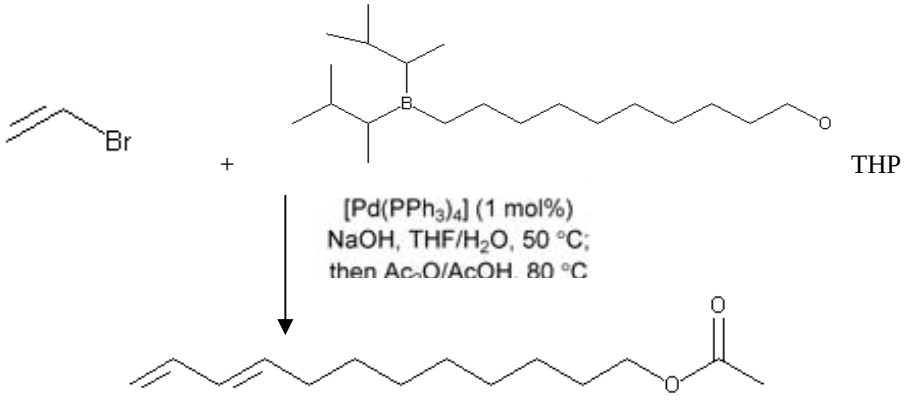
***Mechanism of the Suzuki Coupling***

The basic and most simple mechanism for Suzuki reaction can be studied using palladium as a catalyst. The first step of which is the oxidative addition of palladium to the alkyl halide (designated as 2 in the mechanism) to form an organopalladium species(3), addition of a base to the Reaction gives intermediate(4) via transmetalation [10] , with the boron-ate complex (6) forms an organopalladium species (8). The desired product (9) is then obtained by reductive elimination and the catalyst (palladium) is restored. This type of mechanism is a type of Heterogenous catalysis.




***Application of Suzuki cross coupling reaction in natural product synthesis***

1) The first ever application of suzuki cross-coupling reaction in natural products synthesis was reported in the year 1981 by Rossi and his coworkers in which an insect pheromone isolated from Diparopsis castanea has been synthesized [11] . [ IUPAC NAME (E)-9,11-dodecadien-1-yl acetate ]

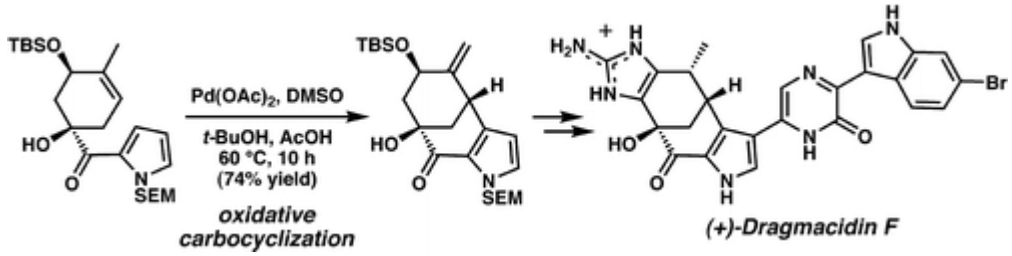



**Synthesis of insect pheromone 121 using suzuki cross coupling reaction**

2) (+)-dynemicin A a potent natural antitumor agent has been successfully synthesized in lab. With a high yield using Suzuki cross coupling reaction.[12]

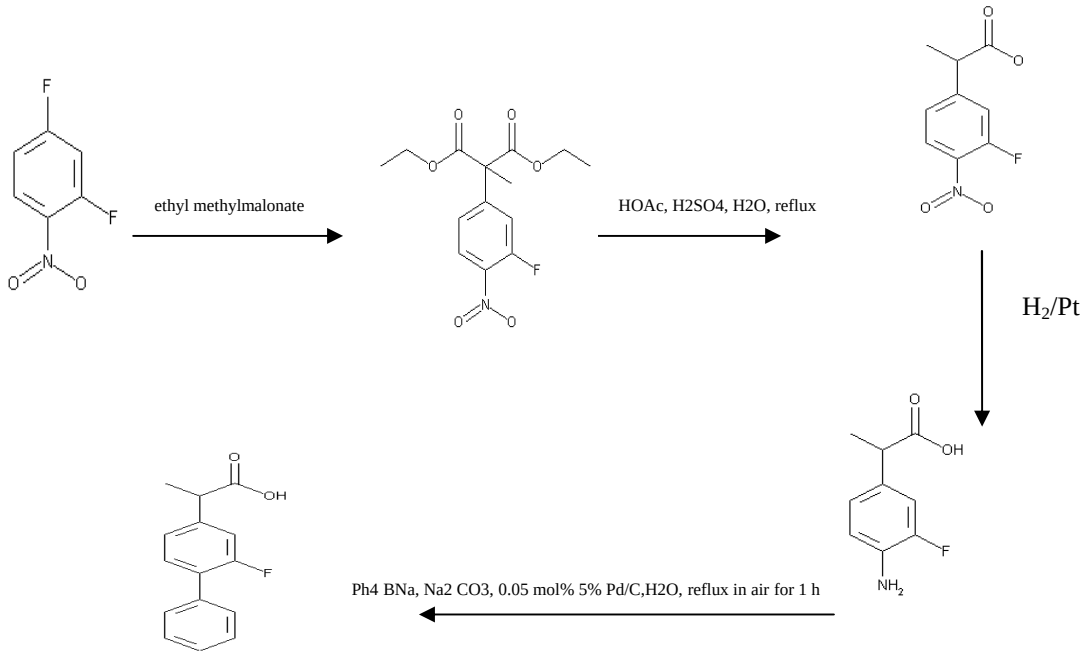
**Structure of (+)-dynemicin A**

3) Suzuki reaction has been successfully used for preparing the antiviral bromoindole alkaloid dragmacidin F which is naturally synthesized in a marine sponge of the genus Halicortex. In vitro studies of dragmacidin F has proved antiviral activity against HSV-1 and HIV 1 virus. [13]

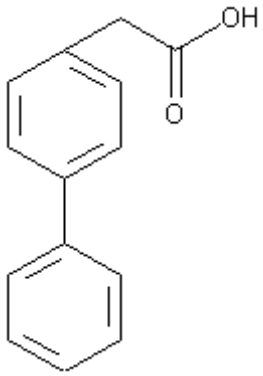



4) *Synthesis of various NSAIDs*

4.1) Flurbiprofen is a commercially available nonsteroidal antiinflammatory and analgesic Drug[14] which is used extensively to treat the inflammation and pain of arthritis[15] has been successfully synthesized using Suzuki cross coupling reaction by using palladium charcoal in water.[16]

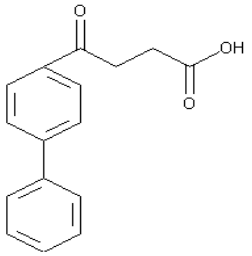


4.2) Felbinac (also known as biphenylylacetic acid) is a topical medicine, belonging to the family of NSAIDs which is used to treat muscle inflammation and arthritis[17] has been also successfully synthesized using cross coupling reaction,



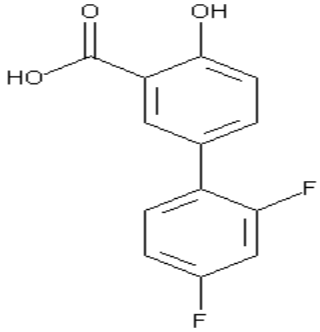

**Structure of Felbinac.**

4.3) Fenbufen a NSAID which is extensively used in the treatment of inflammation in astroarthritis, ankylosing spondylitis and tendinitis, which is also used to relieve backaches, sprains, and fractures[18] has also been synthesized using Suzuki cross coupling reaction.




**Structure of fenbufen**

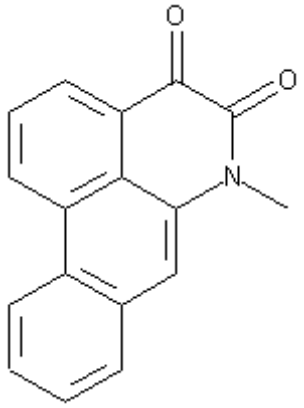
4.4) Difunisal a NSAID which has proven chemical analogs of aspirin[18] has also been synthesized using Suzuki cross coupling reaction.




**Structure of Difunisal**

5) Aporphinoids form an important group of plant secondary metabolites which has been isolated from more than 500 different plant families. It is used in traditional medicine for the treatment of various diseases[19], from benign syndromes to more severe illnesses. Aporphinoids also show display potent cytotoxic activities which may be exploited for the design of anticancer agents. Some

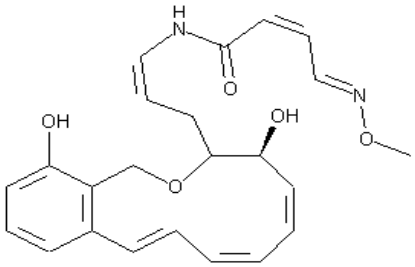
Aporphinoids has also been reported to have antiplatelet and vasorelaxing activity. Suzuki cross coupling reaction able us to prepare such important natural compounds in the lab.




**Structure of 4,5- Dioxo Aporphines (suau et al.)**

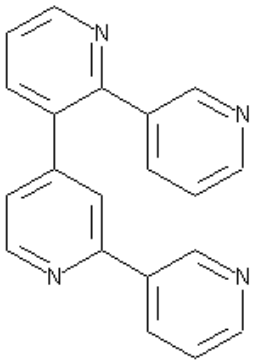
6) Oximidine II

The oximidines are among a family of natural products known as benzolactone enamides. Almost all the compounds in this class of compounds exhibit strong biological potency. Oximidines in particular show antitumor activity and are selective towards mammalian vacuolar type ATP-ases[20]. This compound has also been synthesized suing Suzuki cross coupling reaction.



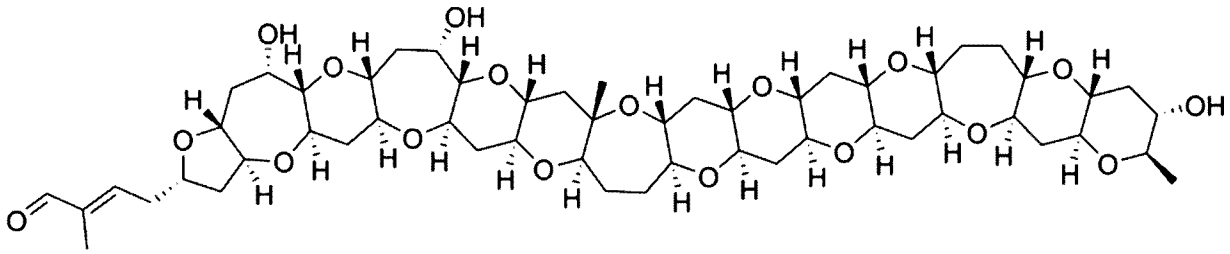

**Structure of oximidine**

7) Nemertelline (a neurotoxic tetra-pyridine compound) which is naturally found in the marinehoplonemertide worm Amphiporus angulatus[21] is used as an anti fouling agent Interest in potential application of this compound as an antifouling agent for boats and other marine installations this is due to this reason that this compound is synthesized for commercial production using Suzuki cross coupling reaction..[22]



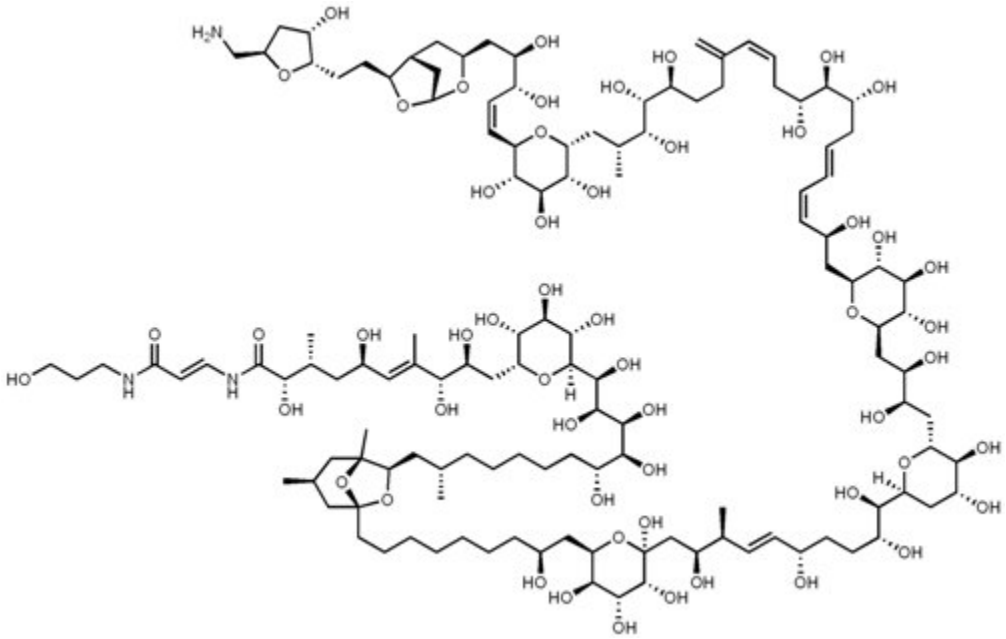

**Structure of Nemertelline**

8) Gymnocin A



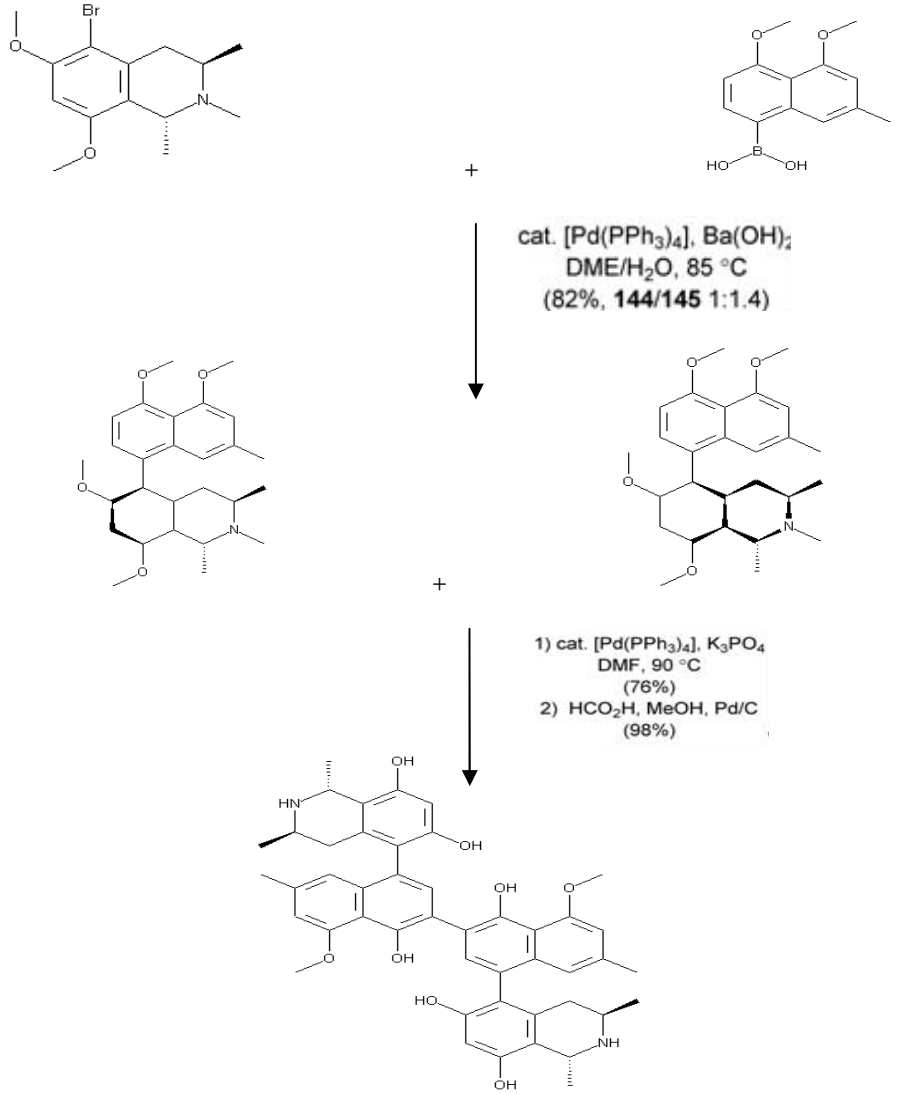
Gymnocin A is present and has been sucessfully isloated from red tide dinoflagellate, Karenia mikimotoi which Contains 14 contiguous rings with two repeating 6/6/7/6/6 systems. gymnocin A contains largest number of rings of polyethers known to date and latest studiestells about the in vitro cytotoxicity against P388 cancer cells[23].

9) Palytoxin is one of the most toxic non-peptide substances known.. Palytoxin is a natural compound that is produced by several marine species and can be found in many more species due to accumulation. Originally it was isolated from a seaweed-like coral commonly known as “seaweed of death from hana” .[24]



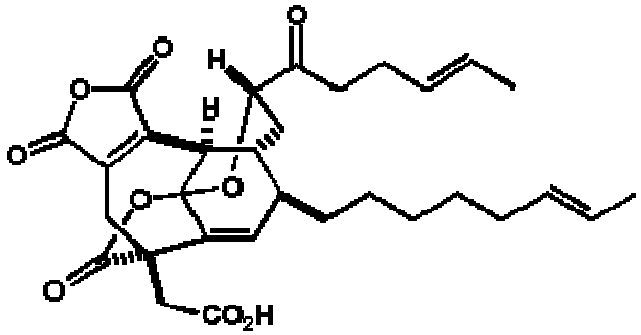
**Structure of palytoxin**

10) Michellamine (an atropisomeric alkaloid)obtained from leaves of Ancistrocladus korupensis[25] has been found to be a strong anti-HIV viral replication inhibitor. Out of 3 michellamines known (Michellamine A, B, and C) , Michellamine B is the most active against the NID-DZ strain of HIV-2[26]. Its lab. synthesis using Suzuki cross coupling reaction has been possible by the collaborative work of Dawson and co-workers[27] which is given as follows



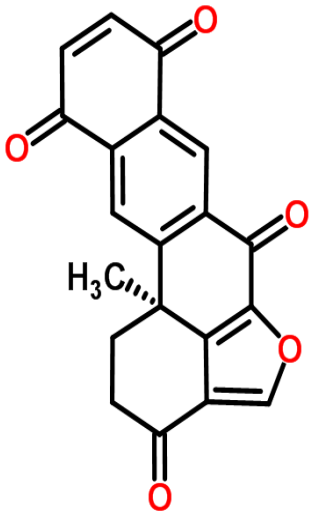

**Synthesis of Michellamine**

11) CP-263,114 a compound which is known for inhibiting squalene synthase inhibitor and Ras farnesylation enzymes[28] has also been synthesized using Suzuki cross coupling reaction.



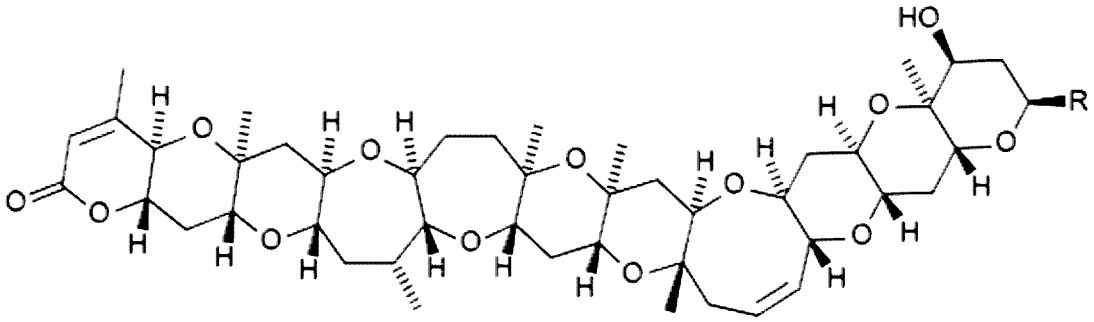
**CP-263,114**

12) Halenaquinone, a chemical compound that inhibits the secondary DNA binding of RAD51 (gene which is known to play an important role on tumor formation) has been synthesized by Shibasaki and co-workers using a number of palladium catalysed reactions.



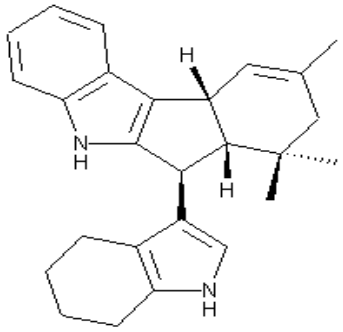
**Halenaquinone**

13) Brevetoxin is a compound produced naturally by a species of dinoflagellate known as karenia brevis are neurotoxins that binds to voltage gated sodium channel in nerve cells, leading to disruption of normal neurological processes[29][30].



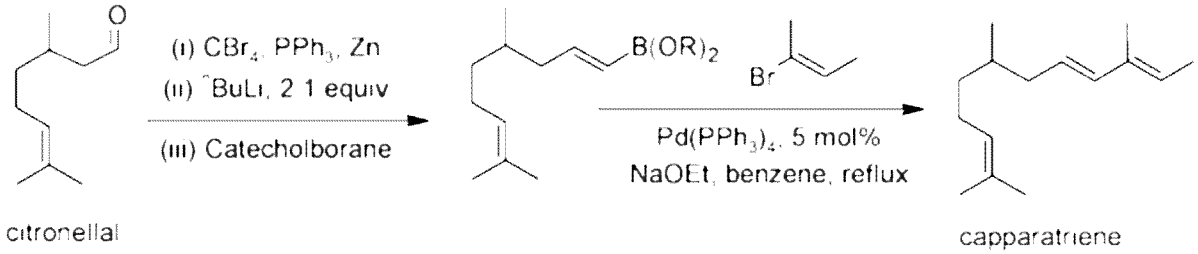
**Structure of Brevetoxin**

14) Yuehchukene isolated from the roots of *Murraya paniculata* and others of the *Murraya* species possesses anti-fertility and estrogenic activities. Has been successfully synthesized by Ishikura and co-workers using Suzuki cross coupling reaction.[31][32][33]



**Structure of Yuehchukene**

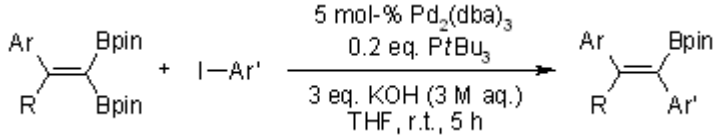
15) The Suzuki coupling has been used for the synthesis of caparratriene using derivatives of cirronellal. Caparratriene so obtained was checked for its pharmacological activity and the compound was found to be highly active against leukemia.[34]



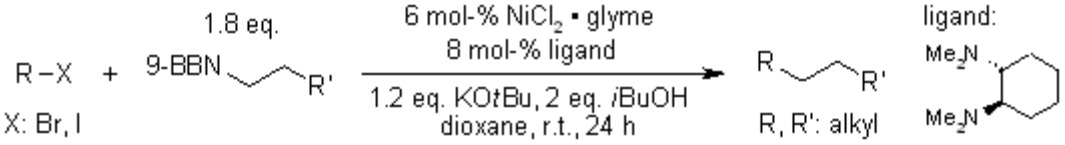

These mentioned molecules are only a few very recent examples. The Suzuki cross coupling has, since its discovery, been used for a large group of different natural products[61].

## *RECENT DEVELOPMENTS*

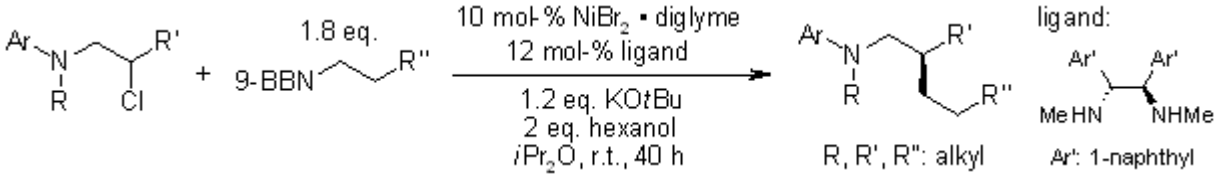
**1)** A highly stereoselective approach for cross coupling reaction between 1,1-diboryl-1-alkenes with electrophiles to form 1,1,2-triaryl-1-alkenes as given by shimizu et al.[35]



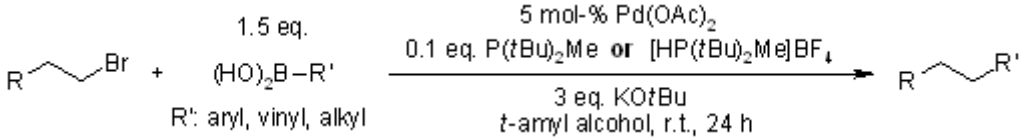

**2)** A successful attempt has been made to make alkyl- alkyl Suzuki cross couples of inactivated secondary alkyl halides at very mild conditions (the reaction also gets to completion even under room temperature)[36]



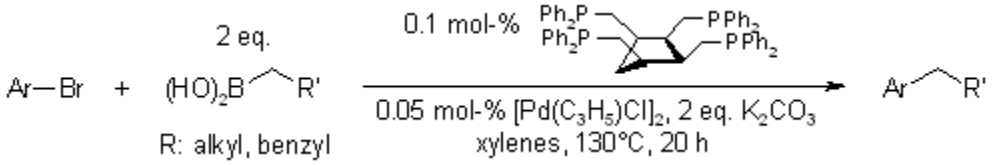
3) Under similar conditions stereoconvergent amine directed alkyl alkyl Suzuki reactions of unactivated secondary alkyl chlorides has been synthesized under similar conditions as mentioned above.[37]



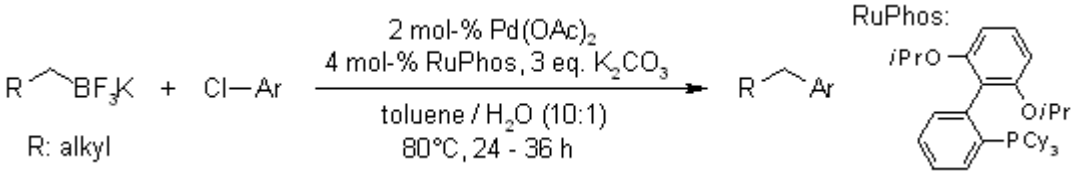

4) To synthesize high order alkane compounds, boronic acids (derivatives of boric acid in which 1 of the –OH group has been replaced by an aryl, vinyl or alkyl group) has been successfully cross coupled with alkyl bromides. The main feature of this reaction is that not only the percentage yield is high but also it requires very mild conditions for the synthesis.[38]



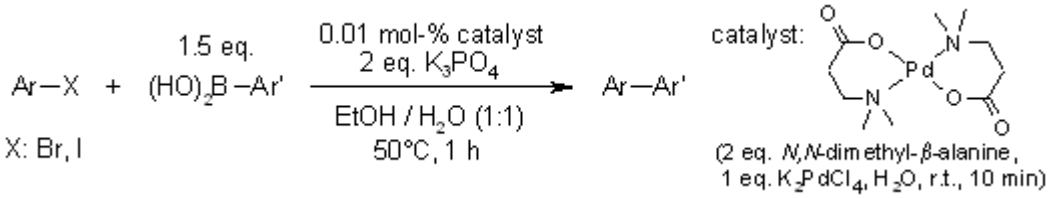

5) To prepare alkyl derivatives of aryl compounds, Suzuki cross coupling reaction has been used in which aryl halides has been cross coupled with alkylboronic acid using tetraphosphine or palladium as a catalyst.[39]



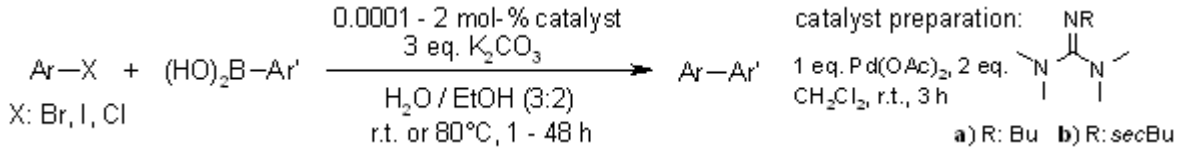

6) In this reaction primary alkyltrifloroborates has been successfully cross coupled with aryl chlorides (reaction known as Suzuki-miyaura cross coupling reaction)[40]



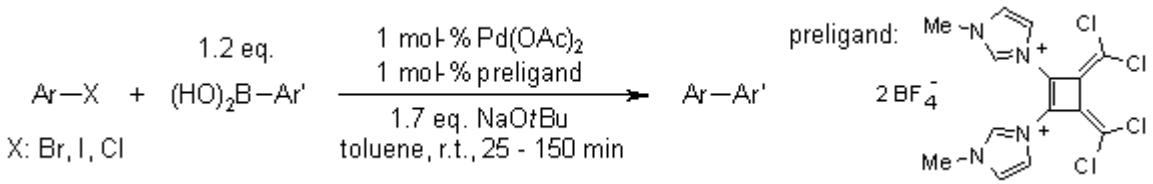

7) For obtaining phosphine free catalyst for Suzuki cross coupling reaction a new lead derivative which is pd(N,N-Dimethyl beta-alaninate)$_2$ has been been synthesized and used as a catalyst.[41]



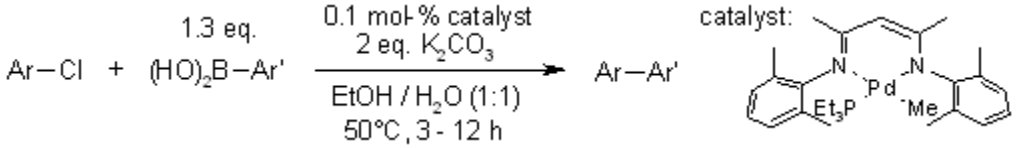
8) For joining two aryl groups with each other (as in fittig reaction), Suzuki cross coupling reaction has been used using guanidine/$Pd(OAc)_2$ as a catalyst which not only gives better results but also can be performed under mild conditions.[42]



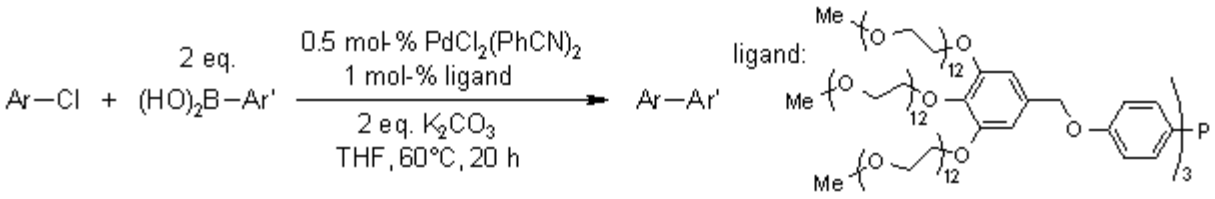

9) A concept of using a precursor for a catalyst in a reaction is relatively new as in majority of cases a catalyst is used directly. In this reaction a precursor ( a cyclobutene-1,2-Bis(imidazolium) salt ) of palladium is used in catalyzing Suzuki – Miyaura reaction which requires no special temperature or pressure conditions for carrying out the reaction.[43]



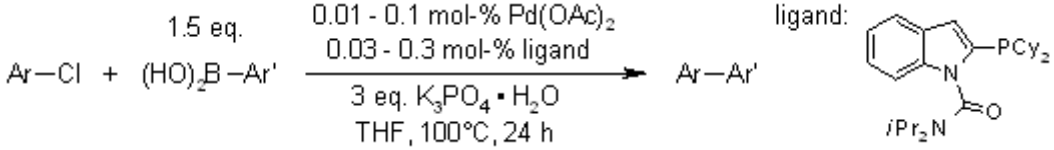

10) A catalyst which is extremely active has been discovered which can be used for the Suzuki-Miryaura Coupling Reactions of aryl chlorides.[44]



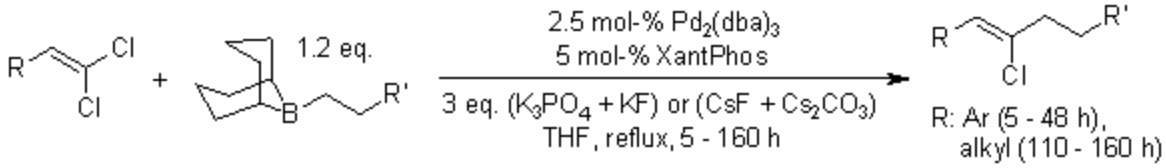

11) An example of enhancing efficiency in the palladium-catalyzed Suzuki-Miyaura Coupling Reaction is shown by a Triarylphosphine Ligand which is bearing a Dodeca (ethylene glycol)chains.[45]



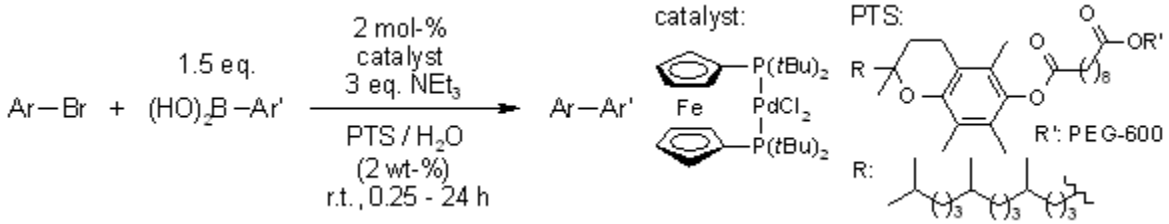

12) A new family of Tunable indolylphosphine Ligands has shown application in Suzuki-Miyauara Coupling of aryl chlorides[46]



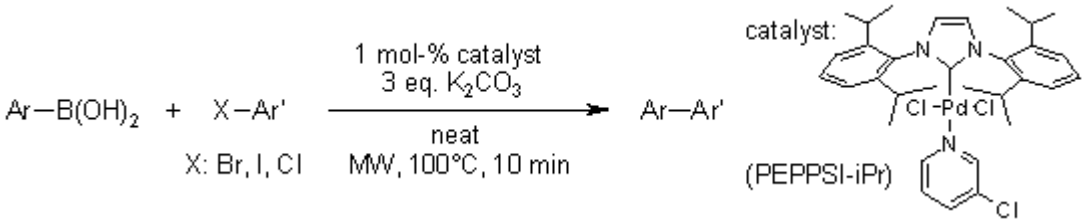
13) Selective Suzuki- Miyaura Monocoupling between 9-alkyl-9-BBN and 1,1-dichloro-1-alkenes yields a good amount of Z-chlorinated internal alkenes using bisphosphine ligands having large P-Pd-P bite angle. Further the transformation of these monochlorinated olefins can be done by introducing stereospecifically trisubstituted olefins.[47]



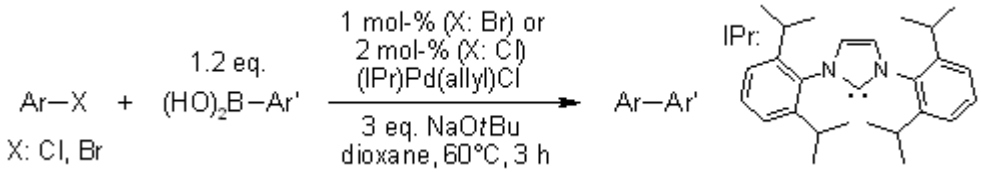

14) Non-ioninc amphiphiles can be used to facilitate Suzuki- Miyaura Couplings at room temperature.[48]



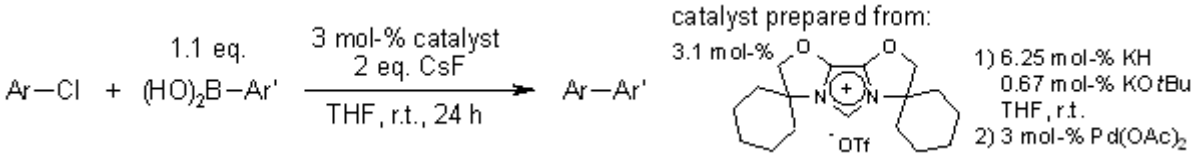

15) PEPPSI-iPr can be used as a catalyst in the solvent-free microwave-assisted Suzuki- Miyaura Coupling.[49]



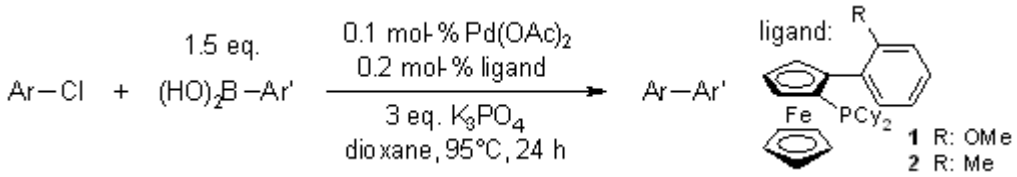

16) Catalyst like (N-Heterocyclic carbene)Pd(allyl)Cl complexes can be used in Cross –Coupling and Dehalogenation Reactions.[50]



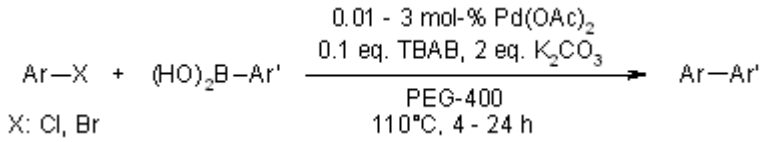

17) Cross-Coupling of sterically hindered Aryl Chlorides can be made possible by using N-Heterocyclic Carbene Ligand having flexible steric bulk at room temperature.[51]



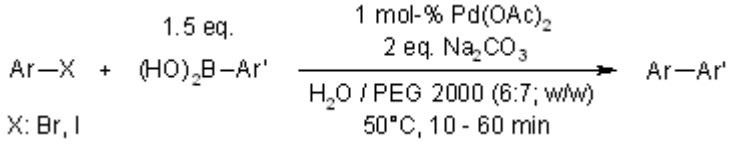
18) Ferrocenyl monophosphine ligands can be used in Suzuki- Miyaura Coupling of Aryl Chlorides.[52]



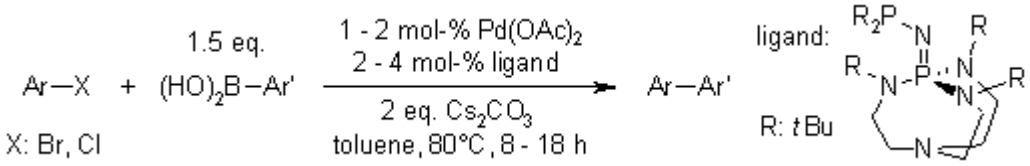

19) pd(OAc)2/TBAB/PEG-400 system has emerged as a reusable and efficient system for the Suzuki- Miyaura Cross –Couplings reactions that are done in ligand-free conditions.[53]



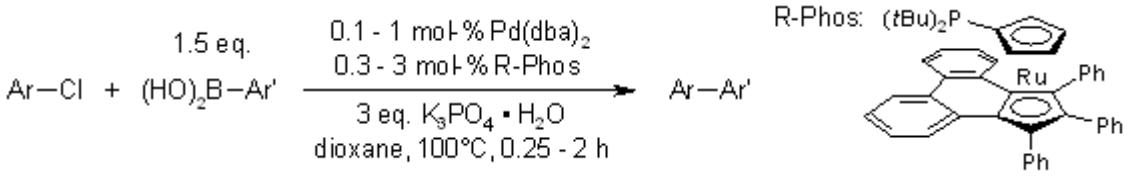

20) Use of catalyst like phosphine-free Palladium acetate in Suzuki- Miyaura reaction in water.[54]



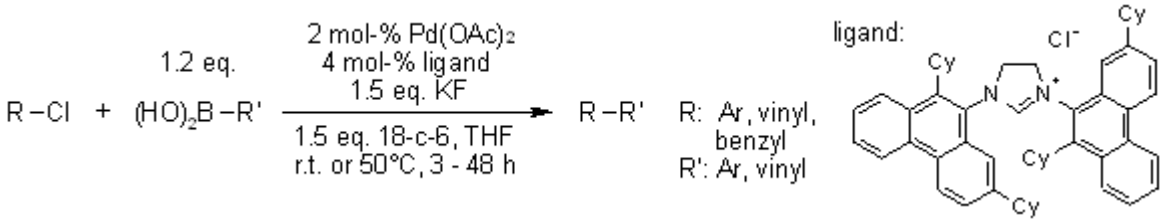

21)$R_2PN=P(^tBuNCH_2CH_2)_3N$ is a new bulky electron rich phosphine which is used for the efficient Pd-assisted Suzuki-Miryaura Cross Coupling Reactions.[55]



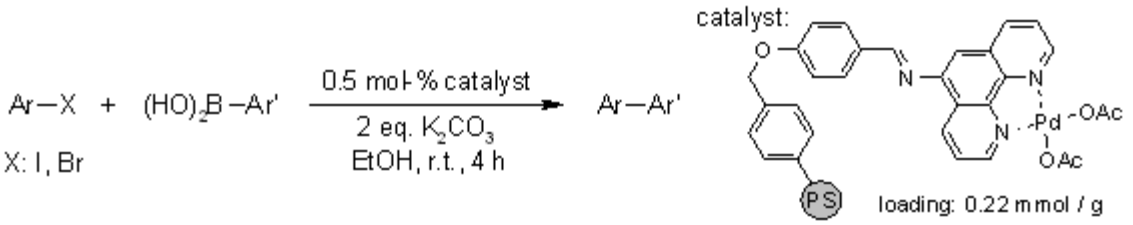

22) Molecule Biphenylene-substituted Ruthenocenylphosphine used for the Suzuki-Miryaura Cross Coupling of Aryl Chlorides.[56]



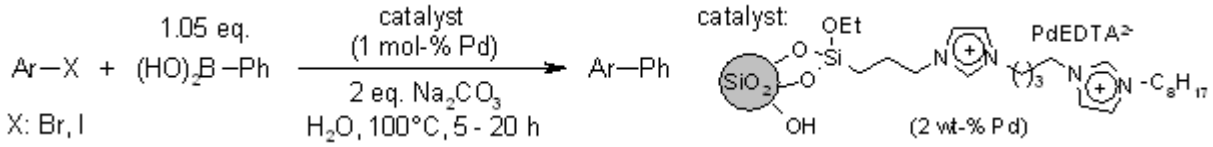

23)Bulky Phenanthryl N-Heterocyclic Carbene ligand used in Paladium catalyzed Suzuki-Miryaura Cross Coupling with aryl chlorides.[57]



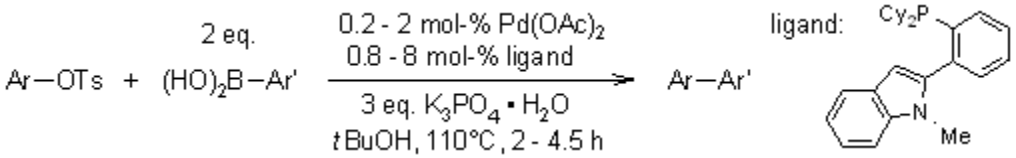

24) Based on a simple Merrifield Resin supported Phenanthroline Palladuim(II) complex recyclable catalysts for Suzuki-Miryaura Cross Coupling Reactions at ambient temperature has been discovered.[58]




25) Highly efficient and reusable catalyst Pd-EDTA which is held in an Ionic Liquid brush can be used in Suzuki-Miryaura reactions in water[59]




26) Catalyst loading reduced to 0.2mol% for the coupling of non activated tosylates by using family of Indolyl phosphine ligands to Suzuki-Miryaura Cross Coupling of aryl tosylates with boric acids, trifluoroborates salts and boronate esters.[60]




## *CONCLUSION*

Suzuki cross coupling reaction is a method for carbon–carbon bond formation which is a highly useful and versatile method needed for the development of modern drug discovery and in the synthesis of many natural products, polymers and other organic compounds . Although the method has found many applications in synthesizing many different molecules, there is still much work to do on the development towards an efficient catalyst applicable for structurally different substrates. There is a need to develop more effective catalyst for the reaction so as to enhance the efficacy and efficiency of the reaction. Also there is an urge to focus on the application of the reaction towards the chemistry of natural products so that the natural products which are pharmacologically important and whose occurrence is limited can be synthesized using this reaction.

## *REFERENCES*


1. Miyaura, Norio; Yamada, Kinji ; Suzuki, Akira (1979). "A new stereospecific cross-coupling by the palladium-catalyzed reaction of 1-alkenylboranes with 1-alkenyl or 1-alkynyl halides". Tetrahedron Letters 20 (36): 3437–3440. doi:10.1016/S0040-4039(01)95429-2.
2. Miyaura, Norio; Suzuki, Akira (1979). "Stereoselective synthesis of arylated (E)-alkenes by the reaction of alk-1-enylboranes with aryl halides in the presence of palladium catalyst". Chem. Comm. (19): 866–867. doi:10.1039/C39790000866.
3. Miyaura, Norio; Suzuki, Akira (1995). "Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds". Chemical Reviews 95 (7): 2457–2483. doi:10.1021/cr00039a007.
4. http://pubs.acs.org/cgi-bin/abstract.cgi/jacsat/2002/124/i46/abs/ja0283899.html
5. N. Miyaura, T. Yanagi, and A. Suzuki. Synth. Commun. 11, 513 (1981).
6. A. Suzuki. Pure Appl. Chem. 57, 1749 (1985).
7. M. Sato, N. Miyaura, and A. Suzuki. Chem. Lett. 1405 (1989).
8. A. Balog, D. Meng, T. Kamenecka, P. Bertinato, D.-S. Su, E.J. Sorensen and S.J. Danishefsky, "Total Synthesis of (–)-Epothilone A" Angew. Chem., Int. Ed. Engl., 1996, 35, 2801. doi:10.1002/anie.199628011 (b) J. Liu, S. D. Lotesta and E. J. Sorensen, "A concise synthesis of the molecular framework of pleuromutilin", Chem. Commun., 2011, 47, 1500. doi:10.1039/C0CC04077K
9. J. Smidt, W. Hafner, R. Jira, J. Sedlmeier, R. Sieber, R. Rüttinger, and H. Kojer, Angew. Chem. 1959, 71, 176.
10. Matos, K.; Soderquist, J. A. J. Org. Chem. 1998, 63, 461–470. (doi:10.1021/jo971681s)
11. R. Rossi, A. Carpita, M. G. Quirici, Tetrahedron 1981, 37, 2617 – 2673.
12. A. G. Myers, N. J. Tom, M. E. Fraley, S. B. Cohen, and D. J. Madar, J. Am. Chem. Soc. 1997, 119, 6072.
13. N. K. Garg, D. D. Caspi, and B. M. Stoltz, J. Am. Chem. Soc. 2004, 126, 9552.
14. J. M. Sha, Yiyao Gongye (Pharmaceutical Industry, in Chinese), 1981, (5), 39.
15. "Medical Dictionary, Houghton Mifflin Company". retrieved July 21, 2010.
16. Gang LU, Robert FRANZÉN, Xiao Jing YU, You Jun XU. Chinese Chemical Letters Vol. 17, No. 4, pp 461-464, 2006. http://www.imm.ac.cn/journal/ccl.html
17. Kohler C, Tolman E, Wooding W, Ellenbogen L. (1980). "A review of the effects of fenbufen and a metabolite, biphenylacetic acid, on platelet biochemistry and function".Arzneimittelforschung 30 (4A): 702–707. PMID 6254545.
18. Adams, S. S. (1999). "Ibuprofen, the propionics and NSAIDs: Personal reflections over four decades". Inflammopharmacology 7 (3): 191–197. doi:10.1007/s10787-999-0002-3. PMID 17638090.
19. Unité d'Analyse Chimique et Physico-Chimique des Médicaments, Université Catholique de Louvain, UCL 72.30-CHAM, Av. E. Mounier 72, 1200 Bruxelles, Belgium.
20. G.A. Molander and F. Dehmel. J. Am. Chem. Soc. 126, 10 313 (2004).
21. Kem, WR; Scott, KN; Duncan, JH (1976). "Hoplonemertine worms -- a new source of pyridine neurotoxins". Experientia 32 (6): 684–6. doi:10.1007/BF01919831.PMID 181266.
22. Bouillon, A; Voisin, AS; Robic, A; Lancelot, JC; Collot, V; Rault, S (2003). "An efficient two-step total synthesis of the quaterpyridine nemertelline". The Journal of Organic Chemistry 68 (26): 10178–80. doi:10.1021/jo034805b. PMID 14682721.
23. http://www.unc.edu/depts/mtcgroup/litmeetings/gymnocina.pdf
24. A) R.W. Armstrong, J.-M. Beau, S. H. Cheon, W. J. Christ, H. Fujioka, W.-H. Ham, L. D. Hawkins, H. Jin, S. H. Kang, Y. Kishi, M. J. Martinelli, W. J. McWhorter, Jr., M. Mizuno, M. Nakata, A. E. Stutz, F. X. Talamas, M. Taniguchi, J. A. Tino, K. Ueda, J.-I. Uenishi, J. B. White, M. Yonaga, J. Am. Chem. Soc. 1989, 111, 7525 – 7530; b) R.W. Armstrong, J.-M. Beau, S. H. Cheon,W. J. Christ, H. Fujioka,W.-H. Ham, L. D. Hawkins, H. Jin, S. H. Kang, Y. Kishi, M. J. Martinelli,W. J. McWhorter, Jr., M. Mizuno, M. Nakata, A. E. Stutz, F. X. Talamas, M. Taniguchi, J. A. Tino, K. Ueda, J.-I. Uenishi, J. B. White, M. Yonaga, J. Am. Chem. Soc. 1989, 111, 7530 – 7533; c) E. M. Suh, Y. Kishi, J. Am. Chem. Soc. 1994, 116, 11205 – 11206.
25. Schlauer, Jan; et al. (1). "Characterization of Enzymes fromAncistrocladus (Ancistrocladaceae) and Triphyophyllum (Dioncophyllaceae) Catalyzing Oxidative Coupling of Naphthylisoquinoline Alkaloids to Michellamines,, ,". Archives of Biochemistry and Biophysics 350 (1): 87–94. doi:10.1006/abbi.1997.0494.
26. Zhang, Heping; Zembower, David. Chen, Zhidong (NaN undefined NaN). "Structural analogues of the michellamine anti-HIV agents. Importance of the tetrahydroisoquinoline rings for biological activity". Bioorganic & Medicinal Chemistry Letters 7 (20): 2687–2690.doi:10.1016/S0960-894X(97)10057-9.
27. K. P. Manfredi, J.W. Blunt, J. H. Cardellina II, J. B. McMahon, L. L. Pannell, G.M. Cragg, M. R. Boyd, J. Med. Chem. 1991, 34, 3402 – 3405; b) M. R. Boyd, Y. F. Hallock, J. H. Cardellina II, K. P. Manfredi, J. W. Blunt, J. B. McMahon, R.W. Buckheit, Jr., G. Bringmann, M. SchUffer, G.M. Cragg, D. W. Thomas, J. G. Jato, J. Med. Chem. 1994, 37, 1740 – 1745.
28. Q. Tan, S. J. Danishefsky, Angew. Chem. 2000, 112, 4683 – 4685; Angew. Chem. Int. Ed. 2000, 39, 4509 – 4511
29. Watkins SM, Reich A, Fleming LE, Hammond R (2008). "Neurotoxic Shellfish Poisoning". Marine Drugs 6 (3): 431–455.
30. Matsuo G, Kawamura K, Hori N, Matsukura H, Nakata T (2004). "Total Synthesis of Brevetoxin-B" (pdf). Journal of the American Chemical Society 126 (44): 14374–14376. doi:10.1021/ja0449269..
31. Bergman, J., Venemalm, L., Total synthesis of Yuehchukene. Tet. Lett., 1988. 29(24): p. 2993-2994.
32. Bergman, J., Venemalm, L., Synthesis of Yuehchukene and some analogues. A general approach. Tet., 1992. 48(4): p. 759-768.
33. M. Ishikura, K. Imaizumi, N. Katagiri, Heterocycles 2000, 53, 553 – 556.
34. Vyvyan, J.R. (1999). "An expedient total synthesis of (+/-)-caparratriene". Tetrahedron Letters 40 (27): 4947–4949. doi:10.1016/S0040-4039(99)00865-5. Retrieved 2008-01-02.
35. M. Shimizu, C. Nakamaki, K. Shimono, M. Schelper, T. Kurahashi, T. Hiyama, J. Am. Chem. Soc., 2005, 127, 12506-12507.
36. B. Saito, G. C. Fu, J. Am. Chem. Soc., 2007, 129, 9602-9603.
37. Z. Lu, A. Wilsily, G. C. Fu, J. Am. Chem. Soc., 2011, 133, 8154-8157.

38. J. H. Kirchhoff, M. R. Netherton, I. D. Hill, G. C. Fu, J. Am. Chem. Soc., 2002, 124, 13662-13663.
39. I. Kondolff, H. Doucet, M. Santelli, Tetrahedron, 2004, 60, 3813-3818.
40. S. D. Dreher, S.-E. Lim, D. L. Sandrock, G. A. Molander, J. Org. Chem., 2009, 74, 3626-3631.
41. X. Cui, T. Qin, J.-R. Wang, L. Liu, Q.-X. Guo, Synthesis, 2007, 393-399.
42. S. Li, Y. Lin, J. Cao, S. Zhang, J. Org. Chem., 2007, 72, 4067-4072.
43. A. Rahimi, A. Schmidt, Synlett, 2010, 1327-1330..
44. D.-H. Lee, M.-J. Jin, Org. Lett., 2011, 13, 252-255.
45. T. Fujihara, S. Yoshida, J. Terao, Y. Tsuji, Org. Lett., 2009, 11, 2121-2124.
46. C. M. So, C. C. Yeung, C. P. Lau, F. Y. Kwong, J. Org. Chem., 2008, 73, 7803-7806.
47. F. Liron, C. Fosse, A. Pernolet, E. Roulland, J. Org. Chem., 2007, 72, 2220-2223.
48. B. H. Lipshutz, T. B. Petersen, A. R. Abela, Org. Lett., 2008, 10, 1333-1336.
49. P. Nun, J. Martinez, F. Lamaty, Synlett, 2009, 1761-1764.
50. O. Navarro, H. Kaur, P. Mahjoor, S. P. Nolan, J. Org. Chem., 2004, 69, 3173-3180.
51. G. Altenhoff, R. Goddard, C. W. Lehmann, F. Glorius, Angew. Chem. Int. Ed., 2003, 42, 3690-3693.
52. C. Baillie, L. Zhang, J. Xiao, J. Org. Chem., 2004, 69, 7779-7782.
53. W.-J. Liu, Y.-X. Xie, Y. Liang, J.-H. Li, Synthesis, 2006, 860-864.
54. L. Liu, Y. Zhang, Y. Wang, J. Org. Chem., 2005, 70, 6122-6125.
55. J. V. Kingston, J. G. Verkade, J. Org. Chem., 2007, 72, 2816-2822.
56. T. Hoshi, T. Nakazawa, I. Saitoh, Y. Mori, T. Suzuki, J.-i. Sakai, H. Hagiwara, S. Akai, Org. Lett., 2008, 10, 2063-2066.
57. C. Song, Y. Ma, Q. Chai, C. Ma, W. Jiang, M. B. Andrus, Tetrahedron, 2005, 61, 7438-7446.
58. J. Yang, P. Li, L. Wang, Synthesis, 2011, 1295-1301.
59. J.-F. Wei, J. Jiao, J.-J. Feng, J. Lv, X.-R. Zhang, X.-Y. Shi, Z.-G. Chen, J. Org. Chem., 2009, 74, 5967-5974.
60. C. M. So, C. P. Lau, A. S. C. Chan, F. Y. Kwong, J. Org. Chem., 2008, 73, 7731-7734.

*Indo Global Journal of Pharmaceutical Sciences( ISSN 2249 1023 ; CODEN-IGJPAI) indexed and abstracted in EMBASE(Elsevier), SCIRUS(Elsevier),CABI, CAB Abstracts, Chemical Abstract Services(CAS), American Chemical Society(ACS), Index Copernicus, EBSCO, DOAJ, Google Scholar and many more. For further details, visit http://iglobaljournal.com*